

REMARKS**I. Claim Status:**

Claims 4-15 are pending and stand rejected. Claims 1, 2 and 16-26 have been canceled previously without prejudice. Claims 4, 12 and 14 have been amended as described more fully herein. Support for the amendment to claim 4 is found in the Specification at pg. 8, lines 19-20, pg. 9, lines 8-13, and more generally throughout the Specification. Support for the amendments to claims 12 and 14 is found throughout the Specification. No new subject matter has been added by the amendments. Entry and consideration are respectfully requested.

II. Restriction Requirement:

Applicants' acknowledge the finality of the restriction requirement. Applicants' reserve the right to re-assert withdrawn claims to the extent a claim deemed generic to both the pending and withdrawn claims is allowed.

III. Claim Objections:

Claim 14 has been objected to as being grammatically unclear. Claim 14 has been amended more particularly point out and distinctly claim that which the Applicants regard as their invention and to address the objection thereby rendering the rejection thereof moot. Reconsideration and removal of the object to claim 14 are respectfully requested.

IV. Rejections Under 35 U.S.C. § 112, Second Paragraph:

Claims 1 and 2 stand rejected under § 112, second paragraph, as being indefinite. Claims 1 and 2 were canceled in Applicants' response to the prior

restriction requirement thereby rendering the current rejections thereof premature. As claims 1 and 2 have been withdrawn by amendment, Applicants respectfully request the § 112, second paragraph, rejections of the claims be withdrawn until such time as claims 1 and 2 are reintroduced via subsequent application.

Claims 12 and 14 stand rejected under § 112, second paragraph, as being indefinite for use of the phrase, "consisting of." Claims 12 and 14 have been amended to recite "comprising" in place of "consisting of." Reconsideration and removal of the rejections of claims 12 and 14 under § 112, second paragraph, are respectfully requested.

V. Rejections Under 35 U.S.C. § 102(e):

Claims 4, 5 and 7-11 stand rejected under § 102(e) as being anticipated by Xu et al. (U.S. 20050112544). Applicants respectfully traverse the rejections.

Xu et al. discloses an apparatus for detecting cells and/or molecules with electrodes. Detection is accomplished by measuring impedance changes due to the presence of cells and/or molecules. See *generally* Abstract. Impedance changes are described as occurring with changes in the population of cells and/or molecules adhering or binding to the electrodes. [0024]. The apparatus uses a series of electrode arrays, each array comprising two or more electrodes separated by non-conductive material and may include a plurality of evenly spaced electrode pairs. [0023-0026]; [0032]; [0192] and [0198]. Notably, electrodes are described throughout the Xu et al. application as being in pairs, at a minimum.

In contradistinction, Applicants' claimed invention, specifically independent claim 4, requires individual electrodes dedicated to individual cells to monitor cells on an individual level rather than as a colony or as a grouping. Xu et al. does not show

or suggest such an electrode configuration. Absent this feature, Xu et al. cannot properly be used to anticipate claim 4. Reconsideration and removal of the rejection of claim 4 are respectfully requested.

Claims 5 and 7-11 depend directly, or ultimately, from claim 4 and are allowable for the same reasons as those given in support of claim 4. Accordingly, reconsideration and removal of the rejection of claims 5 and 7-11 are respectfully requested.

VI. Rejections under 35 U.S.C. § 103(a):

Claims 6 and 15 stand rejected under § 103(a) as being obvious over Xu et al. in view of Sugihara et al. (US 6,132,683). Applicants respectfully traverse the rejections.

Claims 6 and 15 depend ultimately from claim 4 and therefore include all the limitations of claim 4. As stated, the microelectrodes recited in claim 4 are each connected to a single cell and perform electroporation of the cell exclusively from the other microelectrodes. Xu et al. does not show or suggest such a feature. Sugihara et al. is equally deficient for the following reasons.

Sugihara et al. discloses a cell potential measuring electrode assembly that employs reference electrodes separated from other electrodes used to take impedance measurements. The reference electrodes are not introduced to the cell cultures being measured thereby reducing noise and allowing for more precise measurements. [2:35-62]. It is noteworthy that Sugihara et al. is not directed to an assembly for use in cell electroporation.

Sugihara et al. does not disclose, or even suggest, microelectrodes dedicated to individual cells. To the contrary, Sugihara et al. discloses measuring cell

potentials using all the microelectrodes. [2:64-67]. Absent any teaching, suggestion, or motivation to dedicate individual microelectrodes to a single cell so as to perform electroporation of the individual cell, Sugihara et al. does not render claims 6 and 15 obvious alone, or in combination with Xu et al. Accordingly, for all the foregoing reasons, Applicants respectfully request reconsideration and removal of the rejections of claims 6 and 15 under § 103(a).

Claim 12 stands rejected under § 103(a) as being obvious over Xu et al. as applied to claim 11, and further in view of Casnig (US 5,134,070). Applicants respectfully traverse the rejection.

Claim 12 depends ultimately from claim 4 and therefore includes all the limitations of claim 4. As stated, the microelectrodes recited in claim 4 are each connected to a single cell and perform electroporation of the cell exclusively from the other microelectrodes. Xu et al. does not show or suggest such a feature. Casnig is equally deficient for the following reasons.

Casnig discloses a method and device for inducing electroporation of a monolayer of cells. The apparatus includes a Petri-like dish with an electrically-conductive substrate on which the cells are grown. At least one electrode attached to a bottom surface of the substrate provides a conduit for the introduction of electric current to perform the electroporation. Based on the apparatus and method disclosed, the opposing and detection electrodes of Casnig facilitate electroporation, and detection of the effects of electroporation, in a plural, nondiscriminatory manner- all cells are treated as a group or colony rather than on an individual basis. See *generally* Summary of the Invention [3:36-4:19]

Casnig does not disclose, or even suggest, microelectrodes dedicated to individual cells. To the contrary, Casnig discloses measuring cell potentials as a

group using detector microelectrodes. [4:16-19]. Absent any teaching, suggestion, or motivation to dedicate individual microelectrodes to a single cell so as to perform electroporation of the individual cell, Casnig does not render claim 12 obvious alone, or in combination with Xu et al.. Accordingly, for all the foregoing reasons, Applicants respectfully request reconsideration and removal of the rejection of claim 12 under § 103(a).

Claims 13 and 14 stand rejected under § 103(a) as being obvious over Xu et al. as applied to claim 11, and further in view of Gomez et al. (US 2003/0157587). Applicants respectfully traverse the rejection.

Claims 13 and 14 depend ultimately from claim 4 and therefore include all the limitations of claim 4. As stated, the microelectrodes recited in claim 4 are each connected to a single cell and perform electroporation of the cell exclusively from the other microelectrodes. Xu et al. does not show or suggest such a feature. Gomez et al. is equally deficient for the following reasons.

Gomez et al. discloses a method and biochip for collecting a microbiological entity of interest with a non-uniform electric field created by electrically pulsing electrodes in a collection chamber to capture the specimen via dielectrophoresis. Collection electrodes deliver the electric current to capture the desired microbiological entity and may also perform a detection function. In an alternative embodiment, dedicated detection electrodes may be placed in the containment chamber. [0036]. Similar to the other cited references, Gomez et al. does not allocate individual electrodes to individual cells or molecules. It should also be noted Gomez et al. is not directed to electroporation.

Gomez et al. does not disclose, or even suggest, microelectrodes dedicated to individual cells or molecules. To the contrary, Gomez et al. discloses collection

and/or detection electrodes that measure microbiological entities as a group. In fact, Gomez et al. describes using a carrier element disposed on the collection electrodes to entrain the microbiological species and concentrate it at the point of measurement. [0034-0035]. Therefore, Gomez et al. teaches the collection of multiple cells or molecules on a single electrode, which teaches away from Applicants' claimed invention.

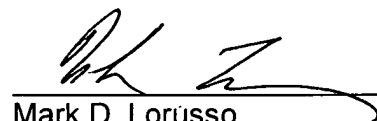
Absent any teaching, suggestion, or motivation to dedicate individual microelectrodes to a single cell so as to perform electroporation of the individual cell, Gomez et al. does not render claims 13 and 14 obvious alone, or in combination with Xu et al.. Accordingly, for all the foregoing reasons, Applicants respectfully request reconsideration and removal of the rejections of claims 13 and 14 under § 103(a).

VII. Conclusion:

For all the foregoing reasons, the claims are considered to define patentably over the prior art. Reconsideration is requested and favorable action is solicited.

Respectfully Submitted,

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